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EXAMINER	
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ART UNIT	**PAPER NUMBER**
1639	

DATE MAILED: 05/04/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/530,907	PAUWELS ET AL.	
	Examiner	Art Unit	
	Mark L. Shibuya	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 April 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-24,26-36 and 38-40* is/are pending in the application.

4a) Of the above claim(s) *8,11-16,19-23 and 38-40* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7,9,10,17,18,24 and 26-36* is/are rejected.

7)☒ Claim(s) *27 and 28* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-24, 26-36, 38-40 are pending. Claims 25, 37 and 41-68 are canceled. Claims 25 and 41-68 were canceled in the Reply to the previous Office action, filed 7/26/2004 (stating, at p. 7, "claim 25 and claims 45-68 have been canceled"; however the listing of the claims shows that claims 25 and 41-68 were canceled thereby). Claims 27 and 28 are objected to. Claims 8, 11-16, **19**, 20-23, 38-40 are withdrawn from consideration, there being no allowable generic claim. Claims 1-7, 9, 10, 17, 18, 24, and 26-36 are examined.

Rejection of Previously Allowed Claims

2. The indicated allowability of claims 2-4 are withdrawn in view of the newly discovered reference(s) to Bjornson et al., US 6,284,113, (rejected under 35 USC 103 below). See MPEP 706.04. Rejections based on the newly cited reference(s) follow.

3. Upon further consideration and search of the prior art, the indication of allowability of claims 2-4, set forth in the final rejection, mailed 10/7/2004, is withdrawn, (see above paragraph). The examiner regrets and apologizes for any inconvenience this may have caused the applicant.

Withdrawal of Final Rejection

4. The finality of rejection of the instant application is withdrawn, in view of the new grounds of rejection of previously allowed claims 2-4. **PROSECUTION IS HEREBY REOPENED.**

Notice of Appeal

5. The notice of appeal, filed 4/6/2005, is acknowledged.

Response to the Amendment After Final Rejection

6. In view of the withdrawal of the finality of rejection, as stated above, applicant's after final amendments to the claims, filed 3/21/2005, are not entered. This is because the claims as amended are not found to be in condition for allowance. Also, the examiner notes that the claims were amended in response to the final rejection, said final rejection now being withdrawn. The following action examines claims 1-7, 9, 10, 17, 18, 24, and 26-36 are examined, as filed 7/26/2004.

Election/Restrictions

7. This application contains claims 8, 11-16, 20-23, 38-40 drawn to an invention nonelected with traverse in Replies to the Requirement for Restriction/Election, filed 6/20/2002, 9/20/2002, and 3/19/2003. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

8. Claim **19** is withdrawn from consideration, in view of applicant's election, entered 4/9/2003, of species of tape or film (as explicitly distinguished from the species of compact disc), in response to the detailed action, mailed 3/19/2003.

Priority

9. The instant application is the national stage of PCT/IB98/01399, filed 9/8/1999.

OBJECTIONS AND REJECTIONS FROM THE PREVIOUS ACTION

Claim Objections

10. Claims 27 and 28 are objected to for depending from canceled claim 25.

Claim Rejections - 35 USC § 112, Second Paragraph

Withdrawn Claim Rejections

11. The rejections of claims 1, 26 and 31 are withdrawn in view of applicant's amendments, filed 7/26/2004.

Maintained Claim Rejections

12. Applicant's argues that the amendments to claims 6, 17-19, 27, and 28, filed 7/26/2004, overcome the rejections of said claims, under 35 U.S.C. 112, second paragraph; this is not persuasive.

Response to Amendments and Arguments

The rejection of claim 6 is maintained because it is unclear how the material allows for spontaneous release of the analytes. The rejections of claims 17-19 are maintained because the amendments to claim 17 are not related to and do not clarify how the elected support of "film or tape" coats a solid support or coats a compact disc (claim 19). The rejection of claims 27 and 28 under 35 U.S.C. 112, second paragraph are maintained because it is still unclear how the "film or tape" can be provided in individually identifiable containers or different compartments.

Claim Rejections

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> **The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.**

13. Claims 6, 7, 17-19, 26-28, and 31 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the

subject matter which applicant regards as the invention. These rejections are necessitated by applicant's amendments to the claims, filed 7/26/2004.

Claim 6, recites the language "wherein the analytes when applied to the solid support are spontaneously released", which renders the claim vague and indefinite, because it is unclear as to from what the analytes are released. This rejection was necessitated by applicant's amendments to the claims, filed 7/26/2004. Likewise, claim 7, recites the language "wherein the analytes when applied to the solid support are controlled released", which renders the claim vague and indefinite, because it is unclear as to from what the analytes are released.

Claim 17 recites the language "the solid support is coated with **a a** layer with molecules", said repeated "a" rendering the claim grammatically incorrect. Likewise, claim 26 recites the language "each analyte is applied to **a a** rod shape", said repeated "a" rendering the claim grammatically incorrect.

Claim 18 recites the language "the solid support is [itself] an information carrier", which renders the claim vague and indefinite because the meaning of "[itself]" is unclear.

Claims 27 and 28 recite the language "[a] method according to claim 25" and "[a] method according to claim 27", respectively, which renders the claims vague and indefinite because claim 25 has been canceled.

Regarding claim 31, the phrase "such as" renders the claim indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention.

See MPEP § 2173.05(d). Furthermore, claim 31 recites the term "drying liquefies", which renders the claim vague and indefinite because the term does not make sense.

Claim Rejections - 35 USC § 112

14. The rejection of claim 31 under 35 U.S.C. § 112, first paragraph, for lacking written description, is withdrawn in view of applicant's amendments and arguments.

Claim Rejections - 35 USC § 102

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

15. Claims 1, 5-7, 9, 10, 17, 24, 26, 29, 30, and 32-36 are rejected under 35 U.S.C. 102(b) as being anticipated by Lerner et al. (US 5,601,992). This rejection is maintained for the reasons of record as set forth in the previous Office action, mailed 3/24/2004.

Response to Arguments

Applicant argues that the reference of Lerner does not teach or suggest all elements of the rejected claims. Applicant argues that the method of Lerner differs from the claimed invention because the claimed invention uses "analytes", not beads. Applicant argues that Lerner et al. discloses using beads, not analytes. Applicant further argues that Lerner fails to inherently anticipate the claimed invention, and cites to MPEP 2112, for the proposition that missing descriptive matter must be necessarily present in the reference. Reply to the previous Office action, at p. 10.

Applicant's arguments filed 7/26/2004 have been fully considered but they are not persuasive. Firstly, the claimed invention uses analytes that are beads, *e.g.*, as in

instant claim 29, which recites: "A method according to Claim 1 wherein the *analytes* are selected from chemical compounds, antigens, antibodies, DNA-probes, cells and *beads* and liposomes carrying an analyte of interest [emphasis added]." Thus the claimed invention uses beads. Secondly, Lerner, at col. 2, lines 16-18, for example, discloses oligomeric molecules, which interact with a target, and that, absent evidence to the contrary, are "analytes" of the claimed invention. Thus, Lerner et al. discloses using analytes. Thirdly, Lerner at col. 3, lines 8-12, for example, teaches "[t]he method includes applying a plurality of beads having multiple copies of the oligomeric molecules associated therewith, to a substrate that is constructed and arranged to permit only localized diffusion of molecules." Because Lerner *expressly* teaches all of the elements of the inventions of claims, as demonstrated above, applicant's argument that Lerner fails to inherently anticipate the claimed invention, is not persuasive.

It is noted that amended claim 17 now recites the limitation that the solid support is coated with a "layer with molecules", which reads on practically any solid support. Also, amended claim 31 is drawn now to methods comprising solvents that include "natural and synthetic polymers", which reads on proteins, nucleic acids, etc., that are naturally found in culture media, as taught in col. 5, line 55-col. 26, line 52, of Lerner.

NEW REJECTIONS OF THE INSTANT ACTION

New Claim Rejections - 35 USC § 112, Second Paragraph

16. Claims 2-4 and 31 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Regarding claim 2, the phrase "in such a manner" renders the claim indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

Regarding claim 31, the phrase "such as" renders the claim indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention. See MPEP § 2173.05(d). Claim 31 recites the limitation " said chemical or physical parameter" in the last line. There is insufficient antecedent basis for this limitation in the claim. It is unclear as to whether the solvent of claim 31 includes all of the compounds listed (such as gelatin, agar, methylcellulose, etc.) collectively, or as single components.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

17. Claims 1-7, 9, 10, 17-19, 24, and 26-36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lerner et al. (US 5,601,992) and Bjornson et al., (US 6,284,113 B1, priority to 19 September 1997).

The claims are drawn to methods for screening of analytes, comprising the steps of: a) simultaneously applying a plurality of analytes to be screened onto at least one solid support such that the analytes remain isolated from one another; b) contacting said at least one analyte-carrying solid support with targets provided in a semi-solid or liquid medium, whereby said analytes are released from the at least one solid support to the targets; and c) measuring analyte-target interactions.

The claims are further drawn to methods according to Claim 1, wherein step (a) comprises (i) disposing the analytes within individually identifiable containers, and (ii) transferring the analytes from the containers to the at least one solid support in such a manner as to maintain the transferred contents of each container separate from those of each other container, (as in claim 2); wherein the individually identifiable containers are an array of capillary tubes, including capillary tubes, pens, including plotter pens, and print heads, (as in claim 3); wherein the individually identifiable containers are an array of capillary tubes each of which is identifiable according to its position within the array, and wherein transfer of the analytes to the at least one solid support occurs by dispensing thereof through the open ends of the capillary tubes, (as in claim 4); wherein the solid support is an information carrier which carries information in electronic, magnetic or digitised form, (as in claim 18); wherein each analyte-bearing solid support is contacted in step b) with a target provided from a separate compartment of a multi-compartmented apparatus, (as in claim 27); wherein said compartments are an arrangement of mini-wells in said apparatus, (as in claim 28); and wherein the analyte dissolves in a solvent, wherein said solvent includes gelatin, polysaccharides such as

agar and agarose, natural and synthetic polymers such as methylcellulose, polyacrylamide, hydrogels, gels containing N-isopropylacrylamide, or thermo-sensitive polymers, such that each analyte following application to the solid support and drying, liquefies in response to said chemical or physical parameter, (as in claim 31). The claimed invention is interpreted in view of the rejection under 35 USC 112, Second Paragraph (discussed above in the instant Office action).

Lerner et al., discloses a method that reads on that of the instant claims. Specifically, the reference discloses detecting the interaction between an oligomeric molecule (reading on claimed analyte) and a target (see, e.g. Abstract). In the method of Lerner et al, a plurality of beads containing peptide analytes are applied to a substrate surface and allowed to diffuse therein (see, e.g. column 21, lines 33-66 – "[t]he oligomeric molecules diffuse through the substrate and interact with a target"). This reads on the claimed step b) of releasing the analytes from the solid supports. The reference also reads on step a) of having analytes on at least one solid support in an isolated fashion, see, for example, column 3, lines 5-22). Beads as solid supports are used for the peptide analytes and the interaction tests were run in culture dishes (see, e.g. Examples 1 & 3 of the reference), this reads on the supports recited in the instant claims. The culture dishes of the reference have gels thereon, see, for example, column 29, lines 62-66. This reads on a coated solid support as recited in the instant claims. The peptide analytes and their preparations (see, e.g. Example 1) read on the analytes recited in instant claims 29, 30 and 32. Various cellular targets are also described by the reference (see Example 2 and column 21, line 66 - column 22, line 67) reading on

claim 33. In the reference, pigment dispersion is measured (see, e.g. column 25, line 55 - column 26, line 52); this reads on the limitations of instant claim 36.

Lerner et al. does not teach methods according to Claim 1, wherein step (a) comprises (i) disposing the analytes within individually identifiable containers, and (ii) transferring the analytes from the containers to the at least one solid support in such a manner as to maintain the transferred contents of each container separate from those of each other container, (as in claim 2); wherein the individually identifiable containers are an array of capillary tubes, including capillary tubes, pens, including plotter pens, and print heads, (as in claim 3); wherein the individually identifiable containers are an array of capillary tubes each of which is identifiable according to its position within the array, and wherein transfer of the analytes to the at least one solid support occurs by dispensing thereof through the open ends of the capillary tubes, (as in claim 4); wherein the solid support is an information carrier which carries information in electronic, magnetic or digitised form, (as in claim 18); wherein each analyte-bearing solid support is contacted in step b) with a target provided from a separate compartment of a multi-compartmented apparatus, (as in claim 27); wherein said compartments are an arrangement of mini-wells in said apparatus, (as in claim 28); and wherein the analyte dissolves in a solvent, wherein said solvent includes gelatin, polysaccharides such as agar and agarose, natural and synthetic polymers such as methylcellulose, polyacrylamide, hydrogels, gels containing N-isopropylacrylamide, or thermo-sensitive polymers, such that each analyte following application to the solid support and drying, liquefies in response to said chemical or physical parameter, (as in claim 31).

Bjornson et al., throughout the patent and abstract, teach methods wherein analytes or beads may be disposed within individually identifiable containers within microarray plates, and transferring the analytes or beads from the containers to microarray substrates in such a manner as to maintain the transferred contents of each container separate from those of each other container in the other microarray, (as in claim 2); wherein the microarrays comprise individually identifiable containers are in an array (e.g., col. 19, line 13; col. 20, line 13, Fig.s 6-8) of capillary tubes, including capillary tubes, and channels of capillary dimensions (col. 8, line 64-col. 9, line 4; col. 11, lines 6-10; col. 15, line 40-col. 16, line 67), (as in claim 3); wherein the microarray plates comprise individually identifiable cavity structures, reading on containers, and arrays of capillary channels, reading on capillary tubes, each of which is identifiable according to its position within the microfluidic network plate, and further comprising a array of microfluidic networks, and wherein transfer of the analytes to the at least one solid support occurs by dispensing thereof through apertures that are the open ends of the capillary channels (e.g., Fig. 4A, col. 16, lines 18-54), (as in claim 4); at col., e.g., col. 20, lines 46-53, teach microarray plates reading upon a solid support, wherein the microarray plates are information carriers which carry information in electronic and digitized form, (as in claim 18); wherein each analyte-bearing solid support is contacted in step b) with a target provided from a separate compartment of a microarray plate that is a multi-compartmented apparatus, (as in claim 27); wherein said compartments are an arrangement of mini-wells in said apparatus, (as in claim 28); and at col. 9, lines 23-55, teach electroflow media, reading on solvents, wherein said media includes

polysaccharides, agarose, natural and synthetic polymers such as methylcellulose, polyacrylamide, hydrogels. Bjornson et al., at col. 18, lines 24-61, especially lines 56-59; col. 30, line 56-col. 31, line 14, disclose the manipulation of bead and particles in the channels of their disclosed microfluidic arrays. Bjornson et al. at col. 29, line 66-col. 30, line 14, teach using microfluidic processing for assay that determining specific binding pair members, as in determining an analyte, and including cell surface binding assays, assays for drug discovery and screening, and studies of receptors.

It would have been *prima facie* obvious at the time of the invention for one of ordinary skill in the art to have used methods comprising methods of screening of analytes, comprising applying a plurality of analytes onto solid supports, such that the analytes remain isolated from one another, and wherein the analytes are released after contact of the analyte-carrying solid supports; and wherein the analytes are disposed within individually identifiable containers, and transferring the analytes from the containers to the at least one solid support in such a manner as to maintain the transferred contents of each container separate from those of each other container, (as in claim 2); wherein the individually identifiable containers are an array of capillary tubes, (as in claim 3); wherein the individually identifiable containers are an array of capillary tubes each of which is identifiable according to its position within the array, and wherein transfer of the analytes to the at least one solid support occurs by dispensing thereof through the open ends of the capillary tubes, (as in claim 4); wherein the solid support is an information carrier which carries information in electronic or digitised form, (as in claim 18); wherein each analyte-bearing solid support is contacted in step b) with

a target provided from a separate compartment of a multi-compartmented apparatus, (as in claim 27); wherein said compartments are an arrangement of mini-wells in said apparatus, (as in claim 28); and wherein the analyte dissolves in a solvent, wherein said solvent includes polysaccharides, agarose, natural and synthetic polymers, methylcellulose, polyacrylamide, hydrogels, such that each analyte following application to the solid support and drying, liquefies in response to said chemical or physical parameter, (as in claim 31).

One of ordinary skill in the art would have been motivated to use methods of screening analytes, wherein the analytes are beads comprising oligomeric molecules, wherein the beads are applied to a substrate, as taught by Lerner (see, e.g., Lerner at col. 21, lines 33-43); and wherein the bead/analytes are manipulated in microarray plates that comprise compartments and capillary tubes, wherein the microarray plates are solid supports that are electronic, digital information carriers and further comprising media, as taught by Bjornson above, because Bjornson teaches manipulation of analytes or beads within microarray plates, and Bjornson teaches evaluating analyte binding to cell surfaces, for example, in order to identify specific binding pairs, and so to screen for potential drugs that target cell surface receptors.

One of ordinary skill in the art would have had a reasonable expectation of success in using bead analytes applied onto substrates, wherein those substrates are electronic microarrays comprising compartments, capillary tubes, and media, because, absent evidence to the contrary, beads or particles that release compounds into solution

were known in the medicinal arts and because flowing particles through such arrays, absent evidence to the contrary, were known in the microfluidic arts.

Conclusion

18. Claims 1-7, 9, 10, 17, 18, 24, and 26-36 are rejected.

19. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mark L. Shibuya whose telephone number is (571) 272-0806. The examiner can normally be reached on M-F, 8:30AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on (571) 272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Mark L. Shibuya
Examiner
Art Unit 1639

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PRIMARY EXAMINER